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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,503	09/25/2003	Shigeru Kawano	21581-00256-US1	4338

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EXAMINER	
PAK, YONG D	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,503	KAWANO ET AL.	
	Examiner	Art Unit	
	Yong D. Pak	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 33-37* is/are pending in the application.

4a) Of the above claim(s) *1-11,18 and 33-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/787,746.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see attached*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a divisional of 09/787,746, now abandoned.

The preliminary amendment filed on September 25, 2003, amending claims 16-18 and 33 and canceling claims 19-32, has been entered.

Claims 1-18 and 33-37 are pending. Claims 1-11, 18 and 33-37 are with drawn. Claims 12-17 are under consideration

Election/Restrictions

Applicant's election of Group II (claims 12-17) in the reply filed on April 21, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-11, 18 and 33-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 21, 2006.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

The information disclosure statements (IDS) submitted on January 10, 2006, January 5, 2005 and September 25, 2003 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that the sequences in Figure 1 lack sequence identification numbers. See particularly 37 CFR 1.821(d).

Specification

The disclosure is objected to because of the following informalities: The specification is missing a Brief Description of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74 is required in the specification.

Appropriate correction is required.

Claim Objections

Claims 12 and 15-17 are objected to because of the following informalities:

In claim 12, the conjunction "and" is missing in line 7 (after the property (2)).

In claim 13, the conjunction "and" is missing in line 4 (after the property (5)).

In claim 14, the conjunction "or" is missing in line 3.

In claims 15-17, the names of microorganisms recited in the claims should be italicized. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

Claims 12-17 are rejected under 35 U.S.C. 101 because the claimed invention is directed to a non-statutory subject matter.

Claims 12-17, as written, do not sufficiently distinguish over enzymes as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products, such as being "isolated" or "purified". In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as taught by the specification. See MPEP 2105.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 12 and claims 13 and 15-17 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the phrase "to give". It is not clear to the Examiner how an enzyme is able "to give" a compound. Examiner requests clarification of the above phrase.

Claim 12 and claims 13 and 15-17 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the phrase "reducing ability". A polypeptide that has an "ability" of catalyzing a reaction conveys that the polypeptide catalyzes the reaction under some conditions but may have the same properties under all or other conditions. A polypeptide "able" of exhibiting a given activity may not have such property at all times or that such property is inherent to said polypeptide. Therefore, it is not clear what are those conditions in which the polypeptides has a "reducing ability" as recited in the claim. Examiner requests clarification of the above phrase.

Claim 12 and claims 13 and 15-17 depending therefrom are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 recites the phrase "very low in reducing activity". The metes and bounds of the phrase in the context of the above claim are not clear to the Examiner. It is not clear to the Examiner what is considered as "very low" by the applicants. A perusal of the specification did not provide a clear definition for the above phrase. Without a clear definition, those skilled in the art would be unable to conclude if a polypeptide is "very low in reducing activity" without knowing the metes and bounds of the phrase.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the phrase "an amino acid sequence of SEQ ID NO:1". The metes and bounds of this phrase in the context of the above claim are not clear to the Examiner. It is not clear whether the polypeptide comprises a fragment of SEQ ID NO:1 or the full length of the amino acid sequence of SEQ ID NO:1. A perusal of the specification did not provide the Examiner with a specific definition for the above phrase. As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean that an enzyme comprising "an amino acid of SEQ ID NO:1" encompasses fragments of SEQ ID NO:1. Examiner requests

clarification of the above phrase and suggests amending the claim by replacing "an" with "the" in the above phrase.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the phrase "shown under". The metes and bounds of the phrase in the context of the claims are not clear. It is not clear to the Examiner if the recited amino acid sequence has the amino acid sequence of SEQ ID NO:1 or is a representative member of a genus. Examiner suggests amending the phrase as "the amino acid sequence of SEQ ID NO:1" to clearly indicate that the polypeptide has the amino acid sequence of SEQ ID NO:1.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the phrase "SEQ ID NO:1 in the sequence listing". The recitation of "sequence listing" is redundant. Examiner suggests deleting the phrase "in the sequence listing".

Claims 14-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-17 recite the phrases "derived from the amino acid sequence shown under SEQ ID NO:1", "is derived from *Candida*", "is derived from *Candida maris*" and "is derived from *Candida maris* IFO 10003". The metes and bounds of these phrases are not clear to the Examiner. Literally, while the term "derived" means "to isolate from or obtain from a source", the above term could also mean "to arrive at by reasoning i.e., to deduce or infer" or also as "to produce or obtain from another substance". Therefore, it is not clear to the Examiner either from the specification or form the claims as to what applicants mean by the above phrase. It is not clear to the Examiner whether the enzyme "derived from the amino acid sequence shown under SEQ ID NO:1", "derived from *Candida*", "derived from *Candida maris*" and "derived from *Candida maris* IFO 10003" encompasses a single specific enzyme (SEQ ID NO:1), as in isolated from *Candida maris* IFO 10003, or whether it encompasses recombinants, variants and mutants of SEQ ID NO:10 from any other source and labeled as an enzyme "derived from the amino acid sequence shown under SEQ ID NO:1", "derived from *Candida*", "derived from *Candida maris*" and "derived from *Candida maris* IFO 10003". As applicants have not provided a definition for the above phrase, Examiner has interpreted the claims broadly to mean that an enzyme "derived from the amino acid sequence shown under SEQ ID NO:1", "derived from *Candida*", "derived from *Candida maris*" and "derived from *Candida maris* IFO 10003" encompasses polypeptides which

are recombinants, variants or mutants of any enzyme having the recited properties. Examiner has given the same interpretation while considering the claims for all other rejections. Examiner requests clarification of the above phrases.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims12-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (See rejection of the phrase "derived" under 112, 2nd paragraph)

Claims 12-17 are drawn to (A) a reductase derived from "*Candida*", "*Candida maris*" or "*Candida maris* IFO 10003" and having the properties and characteristics recited in the claims or (B) a reductase derived from SEQ ID NO:1 by deletion, substitution and /or addition of one or more amino acids and having the recited enzymatic activity. The claim encompasses (A) any reductase isolated from any or all source or and having the recited properties, including recombinants, variants and mutants thereof, or (B) any or all mutants, variants and recombinants of SEQ ID NO:1 and having the recited property. Therefore, the claims are drawn to a genus of polypeptides having any structure. The specification only teaches one species, the reductase comprising the amino acid sequence of SEQ ID NO:1 and having the recited

properties. One species is not enough and does not constitute a representative number of species to describe the whole genus and there is no evidence on the record of the relationship between the structure of the reductase of SEQ ID NO:1 and the structure of any recombinants, variants and mutants of any reductase. Therefore, the specification fails to describe a representative species of the genus comprising reductase derived from "*Candida*", "*Candida maris*", "*Candida maris* IFO 10003" or SEQ ID NO:1, including any or all variants, mutants and recombinants thereof.

Given this lack of description of the representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the inventions of claims 12-17.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 12-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the reductase comprising the amino acid sequence of SEQ ID NO:1, does not reasonably provide enablement for (A) any reductase isolated from any or all source or and having the recited properties, including recombinants, variants and mutants thereof, or (B) any or all mutants, variants and recombinants of SEQ ID NO:1 and having the recited property. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 12-17 are drawn to (A) a reductase derived from "*Candida*", "*Candida maris*" or "*Candida maris* IFO 10003" and having the properties and characteristics recited in the claims or (B) a reductase derived from SEQ ID NO:1 by deletion, substitution and /or addition of one or more amino acids and having the recited enzymatic activity. The claim encompasses (A) any reductase isolated from any or all source or and having the recited properties, including recombinants, variants and mutants thereof, or (A) any or all mutants, variants and recombinants of SEQ ID NO:1 and having the recited property. Therefore, the claims are drawn to polypeptides having any structure. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's

amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a reductase isolated from *Candida maris* IFO 10003 having the amino acid sequence of SEQ ID NO:1. It would require undue experimentation of the skilled artisan to make and use the claimed variants, mutants and recombinants of SEQ ID NO:1 or a reductase isolated from any source, including any or all mutants, recombinants or variants thereof. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure, the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass encompasses (1) any reductase isolated from any or all source or and having the recited properties, including recombinants, variants and mutants thereof, or (2) any or all mutants, variants and recombinants of SEQ ID NO:1 and having the recited property, because the specification does not establish: (A) regions of the protein structure which may be modified without affecting its enzymatic activity; (B) the general tolerance of a reductase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including variants, mutants and recombinants of SEQ ID NO:1 or a reductase isolated from any source, including any or all mutants, recombinants or variants thereof. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of variants, mutants and recombinants of SEQ ID NO:1 or a reductase isolated from any source, including any or all mutants, recombinants or variants thereof having the desired biological characteristics recited in the claim is unpredictable and the experimentation left to those skilled in the art is

unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ a novel microorganism. Since the microorganism is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. All the sequences required for its construction has not been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. 112 may be satisfied by a deposit of the microorganism. The specification does not disclose a repeatable process to obtain the microorganism and it is not apparent if the microorganism is readily available to the public. Accordingly, it is deemed that a deposit of the microorganism should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that if applicants have deposited the microorganism, it must be public available. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that: 1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request; 2. upon granting of the patent the strain will be available to the public under the conditions specified in 37 CFR 1.808; 3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and 4. the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States. (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 12-17 are rejected under 35 U.S.C. 102(e) as being anticipated by Hummel et al.

Claims 12-17 are drawn to (A) a reductase derived from "*Candida*", "*Candida maris*" or "*Candida maris* IFO 10003" and having the properties and characteristics recited in the claims or (B) derived from SEQ ID NO:1 by deletion, substitution and /or addition of one or more amino acids and having the recited enzymatic activity.

Hummel et al. (U.S. Patent No. 6,037,158 – form PTO-892) discloses a polypeptide which stereoselectively reduces 5-acetylfuro[2,3-c]pyridine to 5-(1-(R)-hydroxyethyl)furo[2,3-c]pyridine. Further, since applicants do not place any limitation on the structure of the claimed polypeptides, Examiner takes the position that the reductase of Hummel et al. is "derived" from "*Candida*", "*Candida maris*", "*Candida maris* IFO 10003" or SEQ ID NO:1 by deletion, substitution and /or addition of one or more amino. The polypeptide of Hummel et al. also inherently possesses the properties recited in claims 12-13 since the polypeptide of Hummel et al. and the claimed polypeptides have the same material structure and functional characteristics. Since the Office does not have facilities for examining and comparing applicant's reductase with the reductase of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the reductase of the prior art does not possess the same material structure and functional characteristics of the claimed reductase). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Figzgerald* et al., 205 USPQ 594. Therefore, the reference of Hummel anticipates claims 12-17.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak
Patent Examiner 1652

Tekchand Saidha
Primary Patent Examiner 1652